REMARKS

The Office Action dated April 9, 2003 has been received and carefully studied.

The Examiner rejects claims 14-16 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention.

In order to expedite allowance, claims 14-16 have been cancelled.

The Examiner rejects claims 13-19 under 35 U.S.C. §103(a) as being unpatentable over Bussey, U.S. Patent No. 6,011,148. The Examiner states that Bussey teaches a process of ultrafiltration of nucleic acids using differential pressure as a driving force, from a liquid sample by diluting the sample. The Examiner admits that Bussey does not teach fractionation of DNA fragments, but states that the instant application only describes the process of purifying DNA fragments using ultrafiltration with increased recovery by dilution of the sample, even though the application recites the process as "fractionation".

The rejection is respectfully traversed.

Bussey et al. dilutes the sample for diafiltration, not to enhance the recovery of linear nucleic acids by fractionation of the linear nucleic acids by fragment length. The objective of the filtration in Bussey et al. is to eliminate contaminants, it is not to increase the recovery of a solute of interest. The process of the present invention fractionates like species by size. This is nowhere disclosed or suggested by Bussey et al., whose objective is to retain all nucleic acid as retentate.

With particular reference to claims 17-19, Bussey et al. teach away from the invention as claimed, since the stated objective of Bussey et al. is to retain all nucleic acid as retentate. Claims 17-19 expressly require that certain nucleic acids pass through the membrane. Indeed, claims 17-19 expressly require that nucleic acids pass through or are retained depending upon the number of base pairs. This is nowhere disclosed or suggested by Bussey et al.

In addition, by the accompanying amendment, claims 1, 6, 9, 13 and 17 have been amended to clarify the foregoing distinctions. For example, these claims now recite that the liquid sample consists essentially of the linear nucleic acids being fractionated.

The Examiner rejects claims 1-8 under 35 U.S.C. §103(a) as being unpatentable over Bussey in view of WO 00/66723, and claims 9-12 as being unpatentable over Bussey in view of Simon. The Examiner cites Bussey as above. WO 00/66723 is cited for its disclosure of ultrafiltration to dryness of nucleic acid samples with membranes. Simon is cited as disclosing monovalent and bivalent cations for removal of contaminants by centrifugal ultrafiltration. The Examiner concludes that it would have been obvious to filter the Bussey sample to dryness, and to use the Simon cations in the Bussey process.

The rejections are respectfully traversed.

As set forth above, Bussey et al. do not disclose or suggest fractionating by fragment length a liquid sample consisting essentially of linear nucleic acid. Bussey et al. is removing contaminants from nucleic acids and retaining the nucleic acids as retentate. This teaches away from fractionation as claimed. The secondary references do not supply the deficiencies of Bussey et al.

Furthermore, Applicants note that Bussey et al. uses tangential flow filtration, which requires positive pressure, not vacuum.

Reconsideration and allowance are respectfully requested in view of the foregoing amendment and remarks.

Respectfully submitted,

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Listing of Claims

1. (Currently amended) A process for the fractionation, by nucleic acid fragment length, of linear nucleic acids contained in a liquid sample consisting essentially of linear nucleic acids, comprising diluting said liquid sample, contacting the diluted sample with an ultrafiltration membrane to fractionate by fragment length, and subjecting said diluted sample to a pressure differential to filter said diluted sample to dryness.
2. (Original) The process of claim 1, wherein said liquid sample is diluted to 1/3 to 1/5 its initial concentration.
3. (Original) The process of claim 1, wherein said dilution is carried out with a member selected from the group consisting of water, EDTA, trishydrochloride, a mixture of trishydrochloride and sodium EDTA, and trisethylenediaminetriacetic acid.
4. (Original) The process of claim 1, wherein said linear nucleic acid is double stranded DNA or RNA.
5. (Original) The process of claim 1, wherein said pressure differential is a constant pressure differential.
6. (Currently amended) A process for the fractionation, by nucleic acid fragment length, of linear nucleic acids contained in a liquid sample consisting essentially of linear nucleic acids, comprising providing an ultrafiltration membrane having an upstream and a downstream side, diluting said sample, and contacting said membrane with said liquid sample to fractionate said liquid sample by fragment length, and subjecting said liquid sample to a pressure differential having a pressure less than 25 inches of Hg to filter said diluted sample to dryness.

7. (Original) The process of claim 6, wherein said pressure differential is about 10 inches Hg.

8. (Original) The process of claim 6, wherein said pressure differential is a constant pressure differential.

9. (Currently amended) A process for the fractionation, by nucleic acid fragment length, of contaminants in a liquid sample, comprising increasing the concentration of said contaminants by adding to said sample a member selected from the group consisting of nucleic acid condensing agents and monovalent cations, and contacting the sample with an ultrafiltration membrane to fractionate by fragment length, and subjecting said sample to a pressure differential.

10. (Original) The process of claim 9, wherein said nucleic acid condensing agents are selected from the group consisting of manganese, magnesium, hexaminecobalt chloride, spermine, spermadine, and mixtures thereof.

11. (Original) The process of claim 9, wherein said monovalent cations are selected from the group consisting of sodium, potassium and ammonium.

12. (Original) The process of claim 9, wherein said pressure differential is a constant pressure differential.

13. (Currently amended) A process for the fractionation, by nucleic acid fragment length, of linear nucleic acids contained in a liquid sample consisting essentially of linear nucleic acids, comprising diluting said liquid sample, contacting the diluted sample with an ultrafiltration membrane to fractionate by fragment length, and subjecting said diluted

sample to a first pressure, followed by subjecting said diluted sample to a second pressure different from said first pressure.

14. (Cancelled)

15. (Cancelled)

16. (Cancelled)

17. (Currently amended) In a process for the fractionation of linear nucleic acids contained in a liquid sample consisting essentially of linear nucleic acids, in which said liquid sample is subjected to ultrafiltration whereby nucleic acids having a predetermined number of base pairs normally pass through said ultrafiltration membrane using pressure differential as a driving force, the improvement comprising diluting said liquid sample prior to ultrafiltration in order to retain on said membrane said nucelic acids having said predetermined number of base pairs.

18. (Previously presented) The process of claim 17, wherein said predetermined number of base pairs is 300 or less.

19. (Previously presented) The process of claim 17, wherein said dilution is carried out with a member selected from the group consisting of water, EDTA, trishydrochloride, a mixture of trishydrochloride and sodium EDTA, and trisethylenediaminetriacetic acid.